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(71) Applicant (for all designated States except US): **ELI LILLY AND COMPANY** [US/US]; Lilly Corporate Center, Indianapolis, IN 46285 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **DODD, Steven, Witt** [US/US]; 6541 Stafford Trace, Zionsville, IN 46077 (US). **MACE, Kenneth, Francis** [US/US]; 10907 Killington Circle, Fishers, IN 46038 (US). **TRAUTMANN, Michael, Ernst** [DE/DE]; Lilly Forschung GmbH, Essener Strasse 93, D-22419 Hamburg (DE).

(74) Agents: **STEWART, Mark, J.** et al.; ELI LILLY AND COMPANY, Lilly Corporate Center, Indianapolis, IN 46285 (US).

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Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations

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18 December 2003

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: CHRONIC TREATMENT REGIMEN USING GLUCAGON-LIKE INSULINOTROPIC PEPTIDES

(57) Abstract: The present invention encompasses a method of treating a disease by maintaining chronic steady state serum levels of a GLP-1 compound within a specified range.

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INTERNATIONAL SEARCH REPORT

Intern: pplication No
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A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K38/26

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, MEDLINE, BIOSIS, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>KNUDSEN L B ET AL: "Potent derivatives of glucagon-like peptide-1 with pharmacokinetic properties suitable for once daily administration"</p> <p>JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY, WASHINGTON, US, vol. 43, no. 9, 4 May 2000 (2000-05-04), pages 1664-1669, XP002222050</p> <p>ISSN: 0022-2623</p> <p>page 1665, left-hand column, paragraph 1</p> <p>-page 1667, left-hand column, paragraph 3; table 1</p> <p style="text-align: center;">--- -/--</p>	1-17,25, 26



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

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- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *G* document member of the same patent family

Date of the actual completion of the international search

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14/03/2003

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Charles, D

INTERNATIONAL SEARCH REPORT

Internal Application No
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GREIG N H ET AL: "ONCE DAILY INJECTION OF EXENDIN-4 TO DIABETIC MICE ACHIEVES LONG-TERM BENEFICIAL EFFECTS ON BLOOD GLUCOSE CONCENTRATIONS" DIABETOLOGIA, BERLIN, DE, vol. 42, no. 1, January 1999 (1999-01), pages 45-50, XP000971927 ISSN: 0012-186X page 46, left-hand column, paragraph 1 page 48, right-hand column, paragraph 1 page 49, right-hand column, paragraph 3 ---	19-22, 28, 31
E	WO 02 48183 A (MILlicAN ROHN LEE ;RINELLA JOSEPH VINCENT JUNIOR (US); LILLY CO EL) 20 June 2002 (2002-06-20) page 1, line 7 - line 9; claims 1,8,18; example 31; table 12 page 1, line 29 -page 2, line 11 page 3, line 28 -page 5, line 12 page 21, line 9 - line 14 page 24, line 6 -page 25, line 19 ---	1-18, 23-27
E	WO 02 47715 A (RINELLA JOSEPH VINCENT JUNIOR ;LILLY CO ELI (US); NG KINGMAN (US);) 20 June 2002 (2002-06-20) page 1, line 7 - line 9; claims 1,21,22; example 14; table 8 page 3, line 1 -page 4, line 4 page 19, line 5 - line 23 ---	1-18, 23-27
A	DEACON C F ET AL: "Dipeptidyl peptidase IV resistant analogues of glucagon-like peptide-1 which have extended metabolic stability and improved biological activity" DIABETOLOGIA, BERLIN, DE, vol. 41, 1998, pages 271-278, XP002202152 ISSN: 0012-186X page 271, right-hand column, paragraph 1 -page 272, left-hand column, paragraph 1 page 273, right-hand column, paragraph 4 -page 274, left-hand column, paragraph 1 page 275, left-hand column, paragraph 1 page 276, right-hand column, paragraph 1 -page 277, left-hand column, paragraph 1 ---	1-15,25, 26
A	WO 99 43708 A (MADSEN KJELD ;NOVONORDISK AS (DK); HUUSFELDT PER OLAF (DK); KNUDSE) 2 September 1999 (1999-09-02) page 10, line 20 -page 11, line 3; claims 1,24-37 page 17, line 28 -page 29, line 31 page 41, line 1 - line 10 ---	1,14-19

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INTERNATIONAL SEARCH REPORT

Internal application No
PCT/US 01/44698

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 926 159 A (LILLY CO ELI) 30 June 1999 (1999-06-30) page 2, line 49 -page 3, line 54; claims 15-17 page 5, line 56 -page 6, line 9 ---	1-14
A	US 5 977 071 A (GALLOWAY JOHN A ET AL) 2 November 1999 (1999-11-02) cited in the application the whole document ---	1-14
A	EP 1 076 066 A (ZEALAND PHARMACEUTICALS AS) 14 February 2001 (2001-02-14) page 3, line 9 - line 48; claims 1-4 page 9, line 34 - line 43 -----	19-22, 28,31

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 01/44698

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 1-24 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.: 29, 30, 32
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 29,30,32

Present claims 1-13 (partially), 15-17 (partially), 23-26 (partially), 29-30 (completely), 32 (completely) relate to compounds defined by reference to a desirable characteristic or property, namely GLP-1 analog or derivative.

The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the compounds mentioned in the Claims 14, 18 and 19.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 01/44698

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0248183	A	20-06-2002	AU 2860802 A	24-06-2002
			AU 3392902 A	24-06-2002
			AU 3926202 A	24-06-2002
			AU 3938402 A	24-06-2002
			WO 0248192 A2	20-06-2002
			WO 0248183 A2	20-06-2002
			WO 0247715 A2	20-06-2002
			WO 0247716 A2	20-06-2002
WO 0247715	A	20-06-2002	AU 2860802 A	24-06-2002
			AU 3392902 A	24-06-2002
			AU 3926202 A	24-06-2002
			AU 3938402 A	24-06-2002
			WO 0248192 A2	20-06-2002
			WO 0248183 A2	20-06-2002
			WO 0247715 A2	20-06-2002
			WO 0247716 A2	20-06-2002
WO 9943708	A	02-09-1999	AU 3247799 A	15-09-1999
			WO 9943708 A1	02-09-1999
			EP 1056775 A1	06-12-2000
			US 6268343 B1	31-07-2001
			US 2001011071 A1	02-08-2001
			US 2001047084 A1	29-11-2001
			ZA 9901571 A	02-09-1999
EP 0926159	A	30-06-1999	AU 1821899 A	05-07-1999
			BR 9813658 A	10-10-2000
			CA 2315243 A1	24-06-1999
			CN 1281369 T	24-01-2001
			CZ 20002104 A3	15-08-2001
			EP 0926159 A2	30-06-1999
			HR 20000409 A1	31-10-2000
			HU 0100046 A2	28-05-2001
			JP 2002508332 T	19-03-2002
			NO 20003081 A	08-08-2000
			NZ 505182 A	31-05-2002
			PL 341210 A1	26-03-2001
			TR 200001726 T2	23-10-2000
			WO 9930731 A1	24-06-1999
			ZA 9811466 A	14-06-2000
US 5977071	A	02-11-1999	US 5705483 A	06-01-1998
			US 2002165342 A1	07-11-2002
			US 6133235 A	17-10-2000
			US 6410513 B1	25-06-2002
			US 6388053 B1	14-05-2002
			AU 708159 B2	29-07-1999
			AU 2026895 A	03-10-1996
			BR 9503036 A	23-09-1997
			CA 2150080 A1	22-09-1996
			CN 1131674 A	25-09-1996
			CZ 9501321 A3	16-10-1996
			EP 0733644 A1	25-09-1996
			FI 952536 A	22-09-1996
			HU 74729 A2	28-02-1997
			IL 113809 A	26-07-2000
			JP 8269097 A	15-10-1996

INTERNATIONAL SEARCH REPORT

Information on patent family members

Internat Application No

PCT/US 01/44698

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5977071	A	NO 952034 A	23-09-1996
		NZ 272186 A	29-01-1997
		PL 308783 A1	30-09-1996
		RU 2147588 C1	20-04-2000
		TW 389769 B	11-05-2000
		ZA 9504141 A	22-11-1996
		CA 2137206 A1	10-06-1995
		EP 0658568 A1	21-06-1995
		JP 7196695 A	01-08-1995
<hr/>			
EP 1076066	A	14-02-2001	EP 1076066 A1
			AU 5966000 A
			CN 1376166 T
			WO 0104156 A1
			EP 1196444 A1
			JP 2003505347 T
<hr/>			